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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,225	02/14/2002	Fernando Donate	38342-178463	6196
30827	7590	04/02/2007	EXAMINER	
MCKENNA LONG & ALDRIDGE LLP 1900 K STREET, NW WASHINGTON, DC 20006			BLANCHARD, DAVID J	
		ART UNIT	PAPER NUMBER	
		1643		
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/02/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/074,225	DONATE ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	David J. Blanchard	1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 28 December 2006.

2a)  This action is FINAL.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 1-5 and 7-55 is/are pending in the application.  
4a) Of the above claim(s) 3,4,16-48 and 50-55 is/are withdrawn from consideration.  
5)  Claim(s) \_\_\_\_\_ is/are allowed.  
6)  Claim(s) 1,2,5,7-15 and 49 is/are rejected.  
7)  Claim(s) \_\_\_\_\_ is/are objected to.  
8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All    b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO/SB/08)  
    Paper No(s)/Mail Date \_\_\_\_\_  
  
4)  Interview Summary (PTO-413)  
    Paper No(s)/Mail Date. \_\_\_\_\_  
5)  Notice of Informal Patent Application  
6)  Other: *Notice to comply.*

## DETAILED ACTION

1. Claims 6 and 56-57 are cancelled.

Claim 1 has been amended. It is noted that the status of claim 10 indicates "currently amended", however, there are no markings to show the changes made.

Claims 3-4, 16-48 and 50-55 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

2. Claims 1-2, 5, 7-15 and 49 are under consideration.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

### ***Objections/Rejections Withdrawn***

5. The objection to the first line of the specification as lacking a benefit claim to U.S. Provisional Application Serial No. 60/268,370, filed 02/14/2001 is withdrawn in view of the amendment filed 12/28/2006.

6. The objection to the specification as containing a misplaced phrase at pg. 28 is withdrawn in view of the amendment filed 12/28/2006.

7. The objection to the specification in the use of trademarks is withdrawn in view of applicants' remarks and upon further consideration.

8. The rejection of claims 1-2, 11, 13 and 49 under 35 U.S.C. 102(b) as being anticipated by Borza et al [a] (Biochemistry, 35:1925-1934, 1996, Ids reference #2, filed 6/6/02) is withdrawn in view of the amendments to the claims and applicant's arguments.

9. The rejection of claims 1-2, 5, 7-15 and 49 under 35 U.S.C. 103(a) as being unpatentable over Borza et al [a] (Biochemistry, 35:1925-1934, 1996, Ids reference #2, filed 6/6/02) in view of Azizkhan et al (Journal of Experimental Medicine, 152(4):931-944, 1 October 1980, cited on PTO-892 mailed 7/7/2005) and Borza et al [b] (The Journal of Biological Chemistry, 273(10):5493-5499, 1998, Ids filed 6/6/02) and Simantov et al (US 2001/0041670 A1, 12/6/1999, cited previously on PTO-892 mailed

11/17/2004) is withdrawn in view of the amendments to the claims and applicant's arguments.

***Response to Arguments***

10. The objection to the specification because it contains embedded hyperlinks and/or other form of browser-executable code is maintained.

The examiner acknowledges applicants amendment filed 12/28/2006, however, only one of the two embedded hyperlinks on pg. 15 has been corrected. See pg. 15, lines 12 and 16.

11. The objection to the oath or declaration as being defective as lacking the citizenship of inventor Fernando Donate is maintained.

The response filed 12/28/2006 states that applicant will file a substitute Declaration under separate cover in the name of the indicated inventor showing his citizenship. The examiner acknowledges applicant's intent to file a substitute Declaration, however, no substitute Declaration has been filed and as such the objection is maintained.

12. The rejection of claims 1, 5, 7-15 and 49 under 35 U.S.C. 103(a) as being unpatentable over Borza et al [a] (Biochemistry, 35:1925-1934, 1996, Ids reference #2, filed 6/6/02) in view of Azizkhan et al (Journal of Experimental Medicine, 152(4):931-944, 1 October 1980, cited on PTO-892 mailed 7/7/2005) and Borza et al [b] (The Journal of Biological Chemistry, 273(10):5493-5499, 1998, Ids filed 6/6/02) and Simantov et al (US 2001/0041670 A1, 12/6/1999, cited previously on PTO-892 mailed 11/17/2004).

The response filed 12/28/2006 states that this rejection is based on the interpretation of claim 1 as discussed in the section concerning the 102 rejection over

Borza-1 (Borza et al [a]) and applicants reiterate their earlier remarks concerning the first obviousness rejection. Applicant also states that in view of the amendment of claim 1, the claims are free of Borza-1, and thereby free of the combination of the additional references. Applicants' arguments have been fully considered but are not found persuasive. The instant obviousness rejection is not based on the same interpretation of claim 1 as anticipated by Borza-1 in the 102 rejection or as set forth in the first obviousness rejection. In both of those rejections the art was applied as reading upon or rendering obvious the addition variant of the pentapeptide consensus subsequence of SEQ ID NO:7 and "having" an additional 1 to 4 amino acids (His, Pro or Gly) where the transitional term "having" was interpreted as open-ended claim language and as such, was anticipated by the human and rabbit H/P domain of the prior art. In contrast to those rejections and as stated in the previous Office Action, "For this rejection, the claims are being interpreted as drawn to an anti-angiogenic polypeptide that is a conservative amino acid variant of the human HPRG H/P domain (SEQ ID NO:5) or the rabbit HPRG H/P domain (SEQ ID NO:6) having..." (pg. 11, middle par. of the previous Office Action). Thus, the relevance of applicants' arguments as applied to a different interpretation of the claims and of the prior art is misplaced. Further, the amendment to claim 1 as pointed to by applicant is limited to the addition variant of the pentapeptide consensus subsequence of SEQ ID NO:7 and does not have any bearing on the conservative amino acid variant of the human HPRG H/P domain (SEQ ID NO:5) or the rabbit HPRG H/P domain (SEQ ID NO:6) as applied in the instant rejection.

Applicant also reiterates their points about the inapplicability of the relevance of the detection of secreted heparin as a marker, and adopted by the Office to the present claims. Applicant argues that HPRG does not mediate its antiangiogenic effects through the binding of heparin or through the modulation of endothelial cell migration. Applicant states that the antiangiogenic activity of HPRG is mediated by binding to cell surface tropomysin – not to heparin, citing Juarez et al for support. Applicant's arguments have been fully considered but are not found persuasive. The art of Juarez et al found that the H/P domain of rabbit HPRG induces apoptosis of activated endothelial cells leading to potent angiogenic affects and apoptosis "may be one of the

mechanisms underlying its antiangiogenic activity." (see abstract). Thus, Juarez establishes that apoptosis is one of the mechanisms through which HPRG mediates its antiangiogenic activity, however, this is not dispositive of other mechanisms or the teachings in the cited references, in fact, Juarez also acknowledges the interaction between the H/P domain of HPRG and heparin (see pg. 5344, 1<sup>st</sup> col. and 2<sup>nd</sup> col, par. preceding Materials and Methods section). Again the cited prior art teaches that heparin stimulates capillary endothelial cell migration, an important component of angiogenesis and the migratory activity of heparin could be blocked by heparin specific antagonists and the H/P domain of HPRG was known to interact and neutralize heparin (see Azizkhan et al and Borza et al [b]). Further, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979). See MPEP 2145.

Thus, the rejection of claims 1, 5, 7-15 and 49 under 35 U.S.C. 103(a) as being unpatentable over Borza et al [a] in view of Azizkhan et al and Borza et al [b] and Simantov et al is maintained.

### ***New Grounds of Objections/Rejections***

#### ***Sequence Requirements***

13. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. the specification contains sequences that are encompassed by the sequences rules and require sequence identifiers (SEQ ID numbers) (see pg. 3,

lines 29-31). Applicants' cooperation is requested in reviewing the entire disclosure to ensure that the application is in sequence compliance.

14. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

15. APPLICANT IS GIVEN THE TIME ALLOTED IN THIS OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six-month statutory period. Direct the response to the undersigned.

16. Claim 10 is objected to in the recitation "claims 8".  
Appropriate correction is required.

17. Claims 2 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 2 recites the limitation "said pentapeptide". There is insufficient antecedent basis for this limitation in the claim. It is unclear which pentapeptide is being referenced in the claim. Is "said pentapeptide" referring to the pentapeptide of SEQ ID NO:8, SEQ ID NO:9 or SEQ ID NO:10?

b. Claim 49 recites the limitation "the binding molecule". There is insufficient antecedent basis for this limitation in the claim. Do the cells express an HPRG-binding molecule or some other "binding molecule"? Amending the claim to recite "cells expressing an HPRG-binding molecule" would overcome this rejection.

18. No claims are allowed.

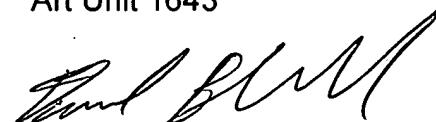
Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Blanchard  
Patent Examiner  
Art Unit 1643

DB  
March 28, 2007



Application No. 10/074,225

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

7. Other: \_\_\_\_\_

**Applicant Must Provide:**

An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

For PatentIn software help, call (703) 308-6856

**PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE**